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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/524,738	09/15/2005	Steffen Goletz	08358.0006	1565

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EXAMINER	
AEDER, SEAN E	

ART UNIT	PAPER NUMBER
1642	

MAIL DATE	DELIVERY MODE
08/04/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/524,738	GOLETZ ET AL.	
	Examiner	Art Unit	
	SEAN E. AEDER	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 May 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *53-60,63-74 and 81-99* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *53-60, 63-74, and 81-99* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

The Amendments and Remarks filed 5/6/08 in response to the Office Action of 2/6/08 are acknowledged and have been entered.

Claims 53-60, 63-74, and 81-99 are pending.

Claims 53 and 95 have been amended by Applicant.

Claims 53-60, 63-74, and 81-99 are currently under examination.

Response to Arguments

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 53, 55, 57, 63, 65, 67, 69, 71, 73, 81-85, 87, 89, 91, 92, 95, 96, and 99 remain rejected under 35 U.S.C. 102(b) as being anticipated by Mivechi (Cancer Research, April 1989, 49: 1954-1958), as evidenced by Lozzio and Lozzio (Blood , March 1975, 45(3): 321-334), for the reasons stated in the Office Action of 2/6/08 and for the reasons set-forth below.

The Office Action of 2/6/08 contains the following text:

"The claims are product-by-process claims drawn to products obtainable by processes involving inducing necrosis of NM-F9 or NM-D4 tumor cells. It is noted that the specification discloses: "The term "NM-F9" (also referred herein as "F9" or "TF-positive F9 cells") or "NM-D4" means cell lines or cells derived from the human myelogenous leukemia cell line K562 (ATCC: CCL-243)" (see last three lines on page 22).

Mivechi teaches vaccine compositions comprising lysates from cells derived from human myelogenous leukemia cell line K562 that have gone through necrosis after being treated at 45C/10 min, 42C/2 hr, or 41C/2 hr see page 1954, in particular). In view of page 22 of the instant specification, the cells taught by Mivechi are NM-F9 and NM-D4 cells. Further, as evidenced by Lozzio and Lozzio, the cells taught by Miyechi are genetically engineered, mutated, or infected by oncogenic viruses (see page 326 of Lozzio and Lozzio, in particular).

Although the combined teachings do not specify the percentage of the tumor cells that are necrotic after induction of necrosis, the percentage of cells expressing membrane-bound HSP 70 protein, or cells treated at 45.5 degrees C, the claimed products appear to be the same as the prior art, absent a showing of unobvious differences. From the data provided in the instant specification (see pages 42-43, in particular), one of skill in the art would expect the products produced by the methods taught by Mivechi et al to be patentably identical to the products recited in the claims. "Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product I in the product-by-process claim I is the same or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re* Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985). See also MPEP 2113. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the products produced by the method of the prior art do not possess the same material and structural characteristics of the claimed products. In the absence of evidence to the contrary, the burden is on Applicant to prove that the claimed products are different from that taught by the prior art and to establish patentable differences. See In re Best 562F .2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2nd 1992 (PTO Bd. Pat. App. & Int. 1989)."

In the Reply of 5/6/08, Applicant amended claims 53 and 95 to include accession numbers for NM-F9 and NM-D4 tumor cell lines and argues that such amendments would obviate this rejection.

The amendments to the claims and the arguments found in the Reply of 5/6/08 have been carefully considered, but are not deemed persuasive. It is acknowledge that claims 53 and 85 have been amended to include accession numbers for NM-F9 and NM-D4 tumor cell lines. *However*, the claimed lysate is not limited to lysate that has been obtained by NM-F9 or NM-D4 tumor cell lines with said accession numbers.

Rather, the claimed lysate is limited to lysate that is "obtainable" by methods using NM-F9 or NM-D4 tumor cell lines with said accession numbers. K562 cells are parental cells of NM-F9 and NM-D4 tumor cell lines with the accession numbers recited in the instant claims. As parental cells of said tumor cell lines, the K562 cells and the NM-F9 and NM-D4 tumor cell lines with the accession numbers recited in the instant claims are comprised of nearly identical matter. Because Mivechi teaches vaccine compositions comprising lysates from K562 cells that have gone through necrosis after being treated at 45C/10 min, 42C/2 hr, or 41C/2 hr (see page 1954, in particular) and because said cells are (1) parental cells of and (2) are comprise of nearly identical matter as the NM-F9 and NM-D4 tumor cell lines with the accession numbers recited in the instant claims, the lysate of Mivechi would *comprise* lysate that is "obtainable" by inducing necrosis of NM-F9 or NM-D4 tumor cell lines with treatment at 45C/10 min, 42C/2 hr, or 41C/2 hr.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 53-60, 67-74, 81-83, 86, and 91-99 remain rejected under 35 U.S.C. 103(a), as being unpatentable over Subjeck et al (US Patent 6,984,384 B1; filed 9/29/00) in view of Yoshima et al (JBC, September 1998, 273(39): 25466-25471), for the reasons stated in the Office Action of 2/6/08 and for the reasons set-forth below.

The Office Action of 2/6/08 contains the following text:

"The claims are product-by-process claims drawn to products obtainable by processes involving inducing necrosis of NM-F9 or NM-D4 tumor cells. It is noted that the specification discloses: "The term "NM-F9" (also referred herein as "F9" or "TF-positive F9 cells") or "NM-D4" means cell lines or cells derived from the human myelogenous leukemia cell line K562 (ATCC; CCL-243)" (see last three lines on page 22).

Subjeck et al teaches a lysate of mutated tumor cells derived from a patient and a composition of said lysate obtainable by a process comprising the steps of: (a) inducing necrosis of tumor cells by subjecting the cells to a temperature of 43C for two hours; and (b) lysing said necrotic tumor cells (see column 19, in particular). It is noted that the instant claims describing lysate as a "pharmaceutical composition" or a "vaccine composition" are merely describing an intended use of the claimed lysate compositions. It is noted that statements of intended purposes or uses are not considered limitations because they merely state an intended use of the invention rather than any distinct definition of any of the claimed invention's limitations (see Pitney Bowes, Inc. v. Hewlett-Packard Co., 182 F.3d 1298, 1305, 51 USPQ2d 1161, 1165 (Fed. Cir. 1999)). Recitation of statements describing the claimed product as a medicament intended to treat a condition are not given patentable weight and are not limitations to the claims. Subjeck et al further teaches compositions comprising immature and mature dendritic cells loaded with the lysate of mutated tumor cells derived from a patient obtainable by a process comprising the steps of: (a) inducing necrosis of tumor cells by subjecting the cells to a temperature of 43C for two hours; and (b) lysing said necrotic tumor cells (columns 26-27, in particular). Subjeck et al further teaches comprising immature and mature dendritic cells loaded with the lysate of mutated tumor cells combined with an adjuvant (column 23, in particular).

Subjeck et al does not specifically teach a product wherein NM-F9 or NM-D4 tumor cells are used to make the product, the percentage of cells necrotic after induction of necrosis, or the percentage of cells expressing membrane-bound HSP 70 protein. However, these deficiencies are made up in the teachings of Yoshima et al.

Yoshima et al teaches cells that are genetically engineered, mutated or infected by oncogenic viruses and derived from the human myelogenous leukemia cell line K562 (see left column of page 25467, in particular). Further, based on the definition of NM-F-9 and NM-D4 tumor cells found in the instant specification (see page 22), the cells taught by Yoshima et al are NM-F9 and NM-D4 tumor cells. Yoshima et al further teaches that HSP 70 expression is undetectable in untreated NM-F-9 and NM-D4 tumor cells (see Figure 1, in particular). Yoshima et al further teaches that HSF1, in response to heat shock, activates expression of HSP70 in NM-F-9 and NM-D4 tumor cells (see right column of page 25466, in particular).

One of ordinary skill in the art at the time the invention was made would have been motivated to use the NM-F9 and NM-D4 tumor cells taught by Yoshimda et al as the mutated tumor cells when producing the vaccine taught by Subjeck et al because Subjeck et al teaches that HSP70 induced by heat shocking tumor cells would function

in a lysed cell vaccine by stabilizing peptides (see column 11, in particular) and Yoshimda et al teaches HSP70 is induced in NM-F-9 and NM-D4 tumor cells upon heat-shock (see right column of page 25466, in particular). One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for using the cells taught by Yoshimda et al as the mutated tumor cells in the vaccine taught by Subjeck et al because Subjeck et al teaches how to use cells to produce said vaccine (see column 19, in particular). Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

Although the combined teachings do not specify the percentage of the tumor cells that are necrotic after induction of necrosis or the percentage of cells expressing membrane-bound HSP 70 protein, the claimed product appear to be the same as the prior art, absent a showing of unobvious differences. From the data provided in the instant specification (see pages 42-43, in particular), one of skill in the art would expect the product produced by the method taught by Subjeck et al to be patentably identical to the products recited in the claims. "Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product I in the product-by-process claim I is the same or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re* Thorpe, 227 USPQ 964, 966 (Fed. Cir. 1985). See also MPEP 2113. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the products produced by the method of the prior art do not possess the same material and structural characteristics of the claimed products. In the absence of evidence to the contrary, the burden is on Applicant to prove that the claimed products are different from that taught by the prior art and to establish patentable differences. See In re Best 562F .2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2nd 1992 (PTO Bd. Pat. App. & Int. 1989)."

In the Reply of 5/6/08, Applicant amended claims 53 and 95 to include accession numbers for NM-F9 and NM-D4 tumor cell lines and argues that such amendments would obviate this rejection.

The amendments to the claims and the arguments found in the Reply of 5/6/08 have been carefully considered, but are not deemed persuasive. It is acknowledge that claims 53 and 85 have been amended to include accession numbers for NM-F9 and NM-D4 tumor cell lines. *However*, the claimed lysate is not limited to lysate that has

been obtained by NM-F9 or NM-D4 tumor cell lines with said accession numbers. Rather, the claimed lysate is limited to lysate that is "obtainable" by methods using NM-F9 or NM-D4 tumor cell lines with said accession numbers. K562 cells are parental cells of NM-F9 and NM-D4 tumor cell lines with the accession numbers recited in the instant claims. As parental cells of said tumor cell lines, the K562 cells and the NM-F9 and NM-D4 tumor cell lines with the accession numbers recited in the instant claims are comprised of nearly identical matter. Because the cited art teaches compositions comprising lysates from K562 cells that have gone through necrosis after treatment and because said cells are (1) parental cells of and (2) are comprise of nearly identical matter as the NM-F9 and NM-D4 tumor cell lines with the accession numbers recited in the instant claims, the lysate of the cited art would *comprise* lysate that is "obtainable" by inducing necrosis of NM-F9 or NM-D4 tumor cell lines with treatment recited in the instant claims.

Claims 53-60, 63-74, and 81-99 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Mivechi (Cancer Research, April 1989, 49: 1954-1958), as applied to claims 53, 55, 57, 63, 65, 67, 69, 71, 73, 81-85, 87, 89, 91, 92, 95, 96, and 99 above, and further in view of Subjeck et al (US Patent 6,984,384 B1; filed 9/29/00), for the reasons stated in the Office Action of 2/6/08 and for the reasons set-forth below.

The Office Action of 2/6/08 contains the following text:

"The claims are product-by-process claims drawn to products obtainable by processes involving inducing necrosis of NM-F9 or NM-D4 tumor cells. It is noted that the specification discloses: "The term "NM-F9" (also referred herein as "F9" or "TF-positive F9 cells") or "NM-D4" means cell lines or cells derived from the human

myelogenous leukemia cell line K562 (ATCC: CCL-243)" (see last three lines on page 22).

The teachings of Mivechi are described above.

Mivechi does not specifically teach dendritic cells loaded with lysates. However, this deficiency is made up in the teachings of Subjeck et al.

The teachings of Subjeck et al are described above.

One of ordinary skill in the art at the time the invention was made would have been motivated to use the NM-F9 and NM-D4 tumor cells taught by Mivechi as the mutated tumor cells when producing the vaccine taught by Subjeck et al because Subjeck et al teaches that HSP70 induced by heat shocking tumor cells would function in a lysed cell vaccine by stabilizing peptides (see column 11, in particular) and Mivechi teaches HSP70 is induced in NM-F-9 and NM-D4 tumor cells upon heat-shock (see left column of page 1955, in particular). One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for using the cells taught by Mivechi as the mutated tumor cells in the vaccine taught by Subjeck et al because Subjeck et al teaches how to use cells to produce said vaccine (see column 19, in particular). Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results."

In the Reply of 5/6/08, Applicant amended claims 53 and 95 to include accession numbers for NM-F9 and NM-D4 tumor cell lines and argues that such amendments would obviate this rejection.

The amendments to the claims and the arguments found in the Reply of 5/6/08 have been carefully considered, but are not deemed persuasive. It is acknowledge that claims 53 and 85 have been amended to include accession numbers for NM-F9 and NM-D4 tumor cell lines. *However*, the claimed lysate is not limited to lysate that has been obtained by NM-F9 or NM-D4 tumor cell lines with said accession numbers. Rather, the claimed lysate is limited to lysate that is "obtainable" by methods using NM-F9 or NM-D4 tumor cell lines with said accession numbers. K562 cells are parental cells of NM-F9 and NM-D4 tumor cell lines with the accession numbers recited in the instant claims. As parental cells of said tumor cell lines, the K562 cells and the NM-F9

and NM-D4 tumor cell lines with the accession numbers recited in the instant claims are comprised of nearly identical matter. Because the cited art teaches compositions comprising lysates from K562 cells that have gone through necrosis after treatment and because said cells are (1) parental cells of and (2) are comprise of nearly identical matter as the NM-F9 and NM-D4 tumor cell lines with the accession numbers recited in the instant claims, the lysate of the cited art would *comprise* lysate that is "obtainable" by inducing necrosis of NM-F9 or NM-D4 tumor cell lines with treatment recited in the instant claims.

Claim Objections

Claim 98 is objected to because of an apparent typographical error. Claim 98 recites: "...the dendritic cells of claim 96...". It is suspected Applicant intended claim 98 to recite: "...the dendritic cells of claim **97** ~~**96**~~...". Proper correction is required.

Summary

No claim is allowed.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SEAN E. AEDER whose telephone number is (571)272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sean E Aeder/
Examiner, Art Unit 1642